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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,568	09/15/2003	Steven Z. Wu	50623.335	2840

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EXAMINER	
SHEIKH, HUMERA N	
ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/663,568	WU ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,28-32 and 34-37* is/are pending in the application.

4a) Of the above claim(s) *36 and 37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,28-32 and 34-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Response after Non-Final Office Action, the Amendment and Applicant's Arguments/Remarks, all filed 02/10/09 is acknowledged.

Applicant has overcome the following rejection by virtue of the amendment to the claims: (1) The 35 U.S.C. §103(a) rejection over Hunter *et al.* (USPN 5,886,026) alone has been withdrawn.

Applicant's arguments regarding the withdrawal of claims 36 and 37 drawn to a non-elected invention (withdrawn by constructive election) was not persuasive. As noted in the Office Action of 11/10/08, the originally claimed invention (claims 25, 27-32, 34 & 35), drawn to a product, does not require that the device be made using the method steps recited in non-elected invention (claims 36 & 37), which requires a solvent extraction process. The device can be made using alternative means. Moreover, the originally-elected invention is drawn to a product, whereas non-elected claims 36 & 37 are drawn to a product-by-process. The different groups would require a separate search in both patent and non-patent data bases and there is no expectation that the searches would be co-extensive in scope. Furthermore, the different groups can be classified in a separate class/subclass and are capable of supporting a separate patent within the art. As a result, there would be a serious search burden upon the Examiner if a restriction/election would not be made. The requirement is still deemed proper and is therefore made FINAL.

Claims 25, 28-32 and 34-37 are pending in this action. Claims 25, 32 and 35 have been amended. Claims 36-37 remain withdrawn (non-elected invention). Claims 1-24, 26, 27 and 33 have been cancelled. Claims 25, 28-32, 34 and 35 remain rejected.

* * * * *

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 25, 28-32, 34 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunter *et al.* (hereinafter "Hunter") (U.S. Patent No. 5,886,026) in view of Wang (U.S. Patent No. 6,379,379).

Hunter ('026) teaches compositions comprising anti-angiogenic factors and polymeric carriers, stents which have been coated with such compositions and methods for utilizing the stents and compositions (see column 1, lines 15-20); (col. 4, lines 25-45); (col. 37, line 31 – col. 38, line 4) and claims. The stents may be self-expanding, balloon expandable or implanted by a change in temperature (col. 23, lines 23-42).

A wide variety of polymeric carriers may be used, including poly(ethylene vinyl acetate), poly(D, L-lactic acid), poly(glycolic acid) and copolymers of poly(caprolactone) or poly(lactic acid) with polyethylene glycol and the like and blends thereof (col. 3, lines 40-64). Polymeric carriers disclosed include both biodegradable and non-biodegradable compositions (col. 16, lines 36-62). The anti-angiogenic compositions may be linked by occlusion in the matrices of the polymer, bound by covalent linkages or encapsulated in microcapsules. In preferred

embodiments, the anti-angiogenic compositions are provided in non-capsular formulations such as microspheres (ranging from nanometers to micrometers in size), as well as pastes, films and sprays (col. 16, line 63 - col. 17, line 11). The sprays may be prepared from microspheres having a size of for example, from 0.1 μm to 3μm (this range falls within and meets Applicant's claimed range of 0.5 to 2 microns in size of instant claim 29) (col. 17, lines 30-65).

In other embodiments of the invention, Hunter teaches that the polymeric carriers are adapted to contain and release a hydrophobic compound, the carrier containing the hydrophobic compound in combination with a carbohydrate, protein or polypeptide. The polymeric carrier contains or comprises regions, pockets of granules or one or more hydrophobic compounds. For example, the hydrophobic compounds may be incorporated within a matrix which contains the hydrophobic compound, followed by incorporation of the matrix within the polymeric carrier. A variety of matrices can be utilized (col. 18, lines 19-53).

Hunter teaches that the stents may be coated with the anti-angiogenic compositions in various manners, including for example: (a) by directly affixing to the stent an anti-angiogenic composition (e.g., by either spraying the stent with a polymer/drug film or by dipping the stent into a polymer/drug solution); (b) by coating the stent with a substance such as a hydrogel which will in turn absorb the anti-angiogenic composition; (c) by interweaving anti-angiogenic factor coated thread (or the polymer itself formed into a thread) into the stent structure; (d) by inserting the stent into a sleeve or mesh which is comprised of or coated with an anti-angiogenic composition; or (e) constructing the stent itself with an anti-angiogenic composition (col. 22, line 8 – col. 23, line 10). Hunter teaches that for vascular stents, the composition should not render the stent thrombogenic (causing blood clots to form) or cause significant turbulence in blood

flow (more than the stent itself would be expected to cause if it was *uncoated*) (see col. 23, lines 2-10).

The anti-angiogenic compositions may additionally comprise a wide variety of compounds in addition to the anti-angiogenic factor and polymeric carrier (col. 15, line 16 - col. 16, line 35).

The manufacturing process of the microspheres and the manufacturing process of the stent coating is discussed at column 45, line 31 – column 48, line 59. Also see column 54, lines 24-51, whereby preparation of control microspheres (drug absent) are discussed.

The figures demonstrate various embodiments of the invention, such as, preparations of microspheres comprising drug (i.e., paclitaxel) made in polymer blend solutions (i.e., EVA/PLA) (col. 6, line 62 - col. 11, line 54).

The instant invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, given the teachings of Hunter. Hunter teaches implantable, expandable stents coated with anti-angiogenic compositions comprising polymeric carriers. The reference teaches that various polymer carriers and blends of polymers can be used. The reference further teaches microspheres that encapsulate the drug (i.e., paclitaxel) and polymer(s) (i.e., EVA/PLA). The reference thus discloses a multi-polymer system for use in coating stents for the treatment and therapy in embolization of blood vessels.

Hunter does not that their coating layer is *free from* any therapeutic substances.

Wang ('379) teaches a stent that includes a polymeric coating or coating(s) on one or both end portions of the stent (see Abstract); (col. 1, line 10 - col. 3, line 17). The coating may

be used as a drug delivery system to treat restenosis, whereby the drugs include radiochemicals to irradiate and prohibit tissue growth (col. 5, lines 32-46). Wang teaches that the stent can have multiple layers of different polymers with the same or different drugs. For example, the stent can have two layers of the same polymer coating (18) with one layer with drug and another layer *without* drugs (col. 6, lines 24-30); (col. 4, lines 46-64).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate coatings that are free of active substance, as taught by Wang within the methods, compositions and devices taught by Hunter. One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Wang explicitly teaches that their stents can have multiple layers of the same polymer coating, whereby one layer has drug incorporated into it, while the other layer is devoid of drug(s), thus providing different polymer coating layers and materials. The expected result would be an enhanced stent for the beneficial treatment of restenosis.

* * * * *

Response to Arguments

Applicant's arguments filed 02/10/09 have been fully considered and were found to be partially persuasive.

- **Rejection under 35 U.S.C. §103(a) over Hunter (USPN 5,886,026) and Wang (USPN 6,379,379):**

Applicant argued, "Claim 25 has been amended to include the limitation that the coating layer is free from any therapeutic substances. As the Examiner admits on page 6 of the Office

action dated November 10, 2008, "Hunter does not [teach or suggest] that their coating layer *is free from* any therapeutic substances." Independent claim 32 also has a similar limitation.

Having a coating layer that is free from any therapeutic substances is important because it allows for greater control of the release of the loaded microparticles containing the therapeutic substance. The use of microparticles allows for higher drug-loading at a particular target site. The Examiner then cites Wang to make up this deficiency by stating that Wang teaches that the stent can have multiple layers of different polymers with the same or different drugs. However, Wang does not teach or suggest the limitations of independent claims 25 (which now incorporates claim 27) and 32.

Claim 25 requires "polymeric particles containing a therapeutic substance embedded within the coating layer, wherein the coating layer comprises a polymer different than the polymer from which the particles are made, wherein the coating layer is free from any therapeutic substances."

Wang teaches the use of multiple-layer coatings, for instance where one layer has a drug and the other layer doesn't have a drug. (See col. 6, 11.26-28). Even if the Examiner makes the argument that claim 25 is not limited to a single layer coating because of the word "comprising" in the claim, Wang fails to teach that one of the layers in the multiple-layer coating has all of the limitations of claims 25 and 32. Thus, Wang fails to teach or suggest claims 25 or 32."

Applicant's arguments have been fully considered and were found to be partially persuasive, based on the amendment to the claims, which incorporates the limitation that the "coating layer is free from any therapeutic substances". Accordingly, the §103(a) rejection over Hunter ('026) alone has been withdrawn. However, the rejection over Hunter in view of Wang ('379) has been maintained. As delineated in the Office Action above, while Hunter does not recognize a coating layer that is free from any therapeutic substances, the secondary reference of Wang is supplied to fill this deficiency of Hunter. Wang sufficiently demonstrates a stent device comprising multiple polymeric layers whereby one layer may incorporate polymer with drug and

the other of the multiple layers may be devoid of or without drugs (see col. 4, lines 46-64 and col. 6, lines 24-30 of Wang). Applicant's argument that "Wang fails to teach that one of the layers in the multiple-layer coating has all of the limitations of claims 25 and 32" was further not persuasive since Wang amply demonstrates the use of the same devices (i.e., stents) which can be formulated both with and without therapeutic substances in combination with the same or different polymeric coating materials. Thus, the art vividly recognizes and teaches stent devices which can be free from active substances as is desired by Applicant. Furthermore, the instant "comprising" claim language does not exclude the use of active agents or substances in the stent device. The "comprising" claim language permits the use of additional components asides from those instantly recited. The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., > Mars Inc. v. H.J. Heinz Co., 377 F.3d 1369, 1376, 71 USPQ2d 1837, 1843 (Fed. Cir. 2004) ("like the term comprising,' the terms containing' and mixture' are open-ended.").< Invitrogen Corp. v. Biocrest Mfg., L.P., 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003).

Applicant's argument that "Having a coating layer that is free from any therapeutic substances is important because it allows for greater control of the release of the loaded microparticles containing the therapeutic substance" is noted. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., greater drug release control) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26

USPQ2d 1057 (Fed. Cir. 1993). Furthermore, it is the position of the Examiner that the Wang reference which clearly demonstrates the use of stent devices having a coating layer free from therapeutic substance would also exhibit greater control or precision of rates of release for the drug-loaded microparticles and thus would provide for the same properties sought by Applicant, absent a showing of evidence to the contrary.

The rejection of record is maintained.

* * * * *

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

This application contains claims 36-37 drawn to an invention nonelected with traverse in the reply filed on 02/10/09. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

--No claims are allowed at this time.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday-Friday during regular business hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Humera N. Sheikh/

Primary Examiner, Art Unit 1615

hns

May 21, 2009